

The differentiation enhancing factors (DEF), comprise at least one each of SH3 consensus binding sequence, ankyrin repeat, pleckstrin homology domain and C2 domain. The DEF induce adipogenesis or neurogenesis; they are mediators of SH3-domain dependent signalling and may be involved in cellular gene expression, cytoskeletal architecture, protein trafficking, endocytosis or adhesion, migration, proliferation and differentiation of cells. Typical applications of DEF and agents that modulate interaction between the protein and it's ligand, or of nucleic acid expressing them, are treatment of hyperplastic and neoplastic disease (a wide range of solid tumours and leukaemias), including metastases; for *in vitro* induction of differentiation of neural crest cells to neurons, glial cells etc.; for increasing neuron survival, and inducing cell repair, in

CC the nervous system (e.g. treatment of traumatic injury, stroke,  
 CC Alzheimer's, Parkinson's or Huntington's diseases, amyotrophic lateral  
 CC sclerosis, multiple sclerosis etc.)  
 XX Sequence 1006 AA;

Query Match 99.6%; Score 5253; DB 2; Length 1006;  
 Best Local Similarity 99.7%; Pred. No. 0;  
 Matches 1003; Conservative 0; Mismatches 3; Indels 0; Gaps 0;

QY 1 MPDQISVSEFVAETHEDYKAPTASSFTTRTAQCNRTVAALDEALDVRMVLKMKKSVKA 60  
 DB 1 MPDQISVSEFVAETHEDYKAPTASSFTTRTAQCNRTVAALDEALDVRMVLKMKKSVKA 60  
 QY 61 INSSGLAHVENEEOYTOALEKFGGNCVCRDDPDLSAFLKFSVFTKELTALFNLIQNMN 120  
 DB 61 INSSGLAHVENEEOYTOALEKFGGNCVCRDDPDLSAFLKFSVFTKELTALFNLIQNMN 120  
 QY 121 NIISFPDLSLLKGLKGVKGLKPKDPKAWKDYETKTKIEKKEKHAHLGHMIRTEISG 180  
 DB 121 NIISFPDLSLLKGLKGVKGLKPKDPKAWKDYETKTKIEKKEKHAHLGHMIRTEISG 180  
 QY 181 AETAEMEKKERRFFQLOMCEYLLKVNKIKKGVDDLQNLKIFHAQCNFFQDGLKAVES 240  
 DB 181 AETAEMEKKERRFFQLOMCEYLLKVNKIKKGVDDLQNLKIFHAQCNFFQDGLKAVES 240  
 QY 241 LKPSITETLSTLHTTKQAQDEERRQLIQRLDILKSAQVEKEDSQIROSTAYSILHQPQG 300  
 DB 241 LKPSITETLSTLHTTKQAQDEERRQLIQRLDILKSAQVEKEDSQIROSTAYSILHQPQG 300  
 QY 301 NKEHGTENGSLYKSDGIRKWKQKSVKNGFLTISHGTANRPPAKNLTLTQVKTNP 360  
 DB 301 NKEHGTENGSLYKSDGIRKWKQKSVKNGFLTISHGTANRPPAKNLTLTQVKTNP 360  
 QY 361 BEKKCFDLISHDRTHYFOAEDEQCOIWMVLSQNSKEALNNAFKGDDNTGENNIVBELT 420  
 DB 361 BEKKCFDLISHDRTHYFOAEDEQCOIWMVLSQNSKEALNNAFKGDDNTGENNIVBELT 420  
 QY 421 KEIISVORTGNDVCCGAPDPTLSTNLGILTCIECSGIIHRELGVHSPQSLTLDV 480  
 DB 421 KEIISVORTGNDVCCGAPDPTLSTNLGILTCIECSGIIHRELGVHSPQSLTLDV 480  
 QY 481 LGTSELLAKNIGNAGNETMECLPAEDSVKPNPGSDMNAKDYITAKVIERYARKKH 540  
 DB 481 LGTSELLAKNIGNAGNETMECLPAEDSVKPNPGSDMNAKDYITAKVIERYARKKH 540  
 QY 541 ADNAAKLHSLCEAVKTRDIFGLLOAVDGVLTETKPLANGHEPDTALHLAVSRVDRTS 600  
 DB 541 ADNAAKLHSLCEAVKTRDIFGLLOAVDGVLTETKPLANGHEPDTALHLAVSRVDRTS 600  
 QY 601 LHVDFLVQNSGNLQKQTKGKSTALHYCCLTDAECLKLLRGKASIEIANESGETPLDI 660  
 DB 601 LHVDFLVQNSGNLQKQTKGKSTALHYCCLTDAECLKLLRGKASIEIANESGETPLDI 660  
 QY 661 AKRLKHECEELLTQALSRFNHSHVYEWRLHEDLDESDDMDKLOPSENREDRP 720  
 DB 661 AKRLKHECEELLTQALSRFNHSHVYEWRLHEDLDESDDMDKLOPSENREDRP 720  
 QY 721 ISFYQLSGNQLQSNVSLARDAANLAKKORAFMPSILQNETYGALLSGSPPPAPAPAS 780  
 DB 721 ISFYQLSGNQLQSNVSLARDAANLAKKORAFMPSILQNETYGALLSGSPPPAPAPAS 780  
 QY 781 TTSAPPLPPRNVGKVQTASSANTLWKNVSVDCGSRSSDDPPAVHPLPLPRLVSTN 840  
 DB 781 TTSAPPLPPRNVGKVQTASSANTLWKNVSVDCGSRSSDDPPAVHPLPLPRLVSTN 840  
 QY 841 PLTPPTPPPVAKTPSWEALSOPEKAPPGISQIRPPPLPPQPSRLPQKPKAPGDKST 900  
 DB 841 PLTPPTPPPVAKTPSWEALSOPEKAPPGISQIRPPPLPPQPSRLPQKPKAPGDKST 900  
 QY 901 PLTNKQPRGPDLSATEALGPLSNAMVLQPPAPMPKRSQATKLKPRVKALYNCVADNP 960  
 DB 901 PLTNKQPRGPDLSATEALGPLSNAMVLQPPAPMPKRSQATKLKPRVKALYNCVADNP 960

QY 961 DELTFSEGDIIVDGEEDQEWIGHIDGDPGRKGAFFVSVFHFIAAD 1006  
 DB 961 DELTFSEGDIIVDGEEDQEWIGHIDGDPGRKGAFFVSVFHFIAAD 1006

## RESULT 2

AAB23647

XX AAB23647 standard; protein; 1006 AA.

XX AAB23647;

XX 05-JAN-2001 (first entry)

XX Human Pap-Delta protein sequence SEQ ID NO:1.

XX Pap; Pyk2 binding protein; Pyk2 C-terminus associated protein; diagnosis;  
 KW cytostatic; neuroprotective; immunomodulatory; cardioactive; cancer;  
 KW cardiovascular disorder; neurodegenerative disorder; immune disorder.  
 XX Homo sapiens.

XX WO200049144-A2.

XX 24-AUG-2000.

XX 18-FEB-2000; 2000WO-US004647.

XX 22-FEB-1999; 99US-0121125P.

XX (SUGEN-) SUGEN INC.

XX Lev S, Schlessinger J, Chen A, Hernandez J, Martinez R;

XX Plowman GD;

XX WPI; 2000-524592/47.

XX Pyk2 binding protein nucleic acids, polypeptides, antibodies and  
 PT antisense oligonucleotides, the oligonucleotides are useful for treating  
 PT cancer or a cardiovascular, neurodegenerative or immune disorder.  
 XX Claim 15; Fig 1; 132pp; English.

XX The present sequence represents the human Pap-Delta protein. Pap is a

XX Pyk2 C-terminal associated protein (Pyk2 binding protein). Pap proteins

XX have cytosolic, neuroprotective, immunomodulatory and cardioactive

XX activities. Pyk2 binding protein polypeptides such as Pap are useful as

XX diagnostic agents for the detection of diseases. Oligonucleotides from

XX polynucleotide sequences encoding Pap proteins may be useful for the

XX treatment of diseases such as cancer or a cardiovascular,

XX neurodegenerative or immune disorder

XX Sequence 1006 AA;

SQ

## Query Match

Best Local Similarity 96.4%; Score 5084; DB 3; Length 1006;

Matches 983; Conservative 0; Mismatches 23; Indels 0; Gaps 0;

QY 1 MPDQISVSEFVAETHEDYKAPTASSFTTRTAQCNRTVAALDEALDVRMVLKMKKSVKA 60  
 DB 1 MPDQISVSEFVAETHEDYKAPTASSFTTRTAQCNRTVAALDEALDVRMVLKMKKSVKA 60  
 QY 61 INSSGLAHVENEEOYTOALEKFGGNCVCRDDPDLSAFLKFSVFTKELTALFNLIQNMN 120  
 DB 61 INSSGLAHVENEEOYTOALEKFGGNCVCRDDPDLSAFLKFSVFTKELTALFNLIQNMN 120  
 QY 121 NIISFPDLSLLKGLKGVKGLKPKDPKAWKDYETKTKIEKKEKHAHLGHMIRTEISG 180  
 DB 121 NIISFPDLSLLKGLKGVKGLKPKDPKAWKDYETKTKIEKKEKHAHLGHMIRTEISG 180  
 QY 181 AETAEMEKKERRFFQLOMCEYLLKVNKIKKGVDDLQNLKIFHAQCNFFQDGLKAVES 240  
 DB 181 AETAEMEKKERRFFQLOMCEYLLKVNKIKKGVDDLQNLKIFHAQCNFFQDGLKAVES 240

QY 241 LKPSIETLSTDLHTI KOAQDEERRQLIQLDRILKSAQVEQKEDSQRSTAYSLSHQPOG 300  
 Db 241 LKPSIETLSTDLHTI KOAQDEERRQLIQLDRILKSAQVEQKEDSQRSTAYSLSHQPOG 300  
 QY 301 NKEHGTNRNGSLYKKSQDGIKRVWOKRCSVKNGLFTTISHGTANRPPAKJNLLTCOVKTNP 360  
 Db 301 NKEHGTNRNGSLYKKSQDGIKRVWOKRCSVKNGLFTTISHGTANRPPAKJNLLTCOVKTNP 360  
 QY 361 EEKCFDLISHDRTHYFQAEDEQECQIWMVSLQNSKEEALNNAFKGDDNTGENNIVQELT 420  
 Db 361 EEKCFDLISHDRTHYFQAEDEQECQIWMVSLQNSKEEALNNAFKGDDNTGENNIVQELT 420  
 QY 421 KEIISEVORMTGNDVCCDCCGAPDPTWLSNLGILTCIECSGIRHRELGVHSPMOSLTLDV 480  
 Db 421 KEIISEVORMTGNDVCCDCCGAPDPTWLSNLGILTCIECSGIRHRELGVHSPMOSLTLDV 480  
 QY 481 LGTSELLAKNIGNAGFNETMECCLPADSDVKNPFGSDMNAKDYITAKYIERRYARKKH 540  
 Db 481 LGTSELLAKNIGNAGFNETMECCLPADSDVKNPFGSDMNAKDYITAKYIERRYARKKH 540  
 QY 541 ADNAAKLHSLCEAVKTRDIFGLLOAYADGVLDLTKIPLANGHEPDETALHLAVRSVDRTS 600  
 Db 541 ACNAAKLHSLCEAVKTRDIFGLLOAYADGVLDLTKIPLANGHEPDETALHLAVRSVDRTS 600  
 QY 601 LHIIVDFLVQNSGNDKQTKGKSTALHYCCCLTDNAECLKLLRGKASIEIANESGETPLDI 660  
 Db 601 LHIIVDFLVQNSGNDKQTKGKSTALHYCCCLTDNAECLKLLRGKASIEIANESGETPLDI 660  
 QY 661 AKRLKHEHCHELTQALSGRPNHSHVHYEWRLHEDLDSDDMDKLOPSENRRDRP 720  
 Db 661 AKRLKHEHCHELTQALSGRPNHSHVHYEWRLHEDLDSDDMDKLOPSENRRDRP 720  
 QY 721 ISFYQLGSLNQNSLARDANLAKKORAFMPSILQNETYCALLSGSPPPAPQAPAS 780  
 Db 721 ISFYQLGSLNQNSLARDANLAKKORAFMPSILQNETYCALLSGSPPPAPQAPAS 780  
 QY 781 TTSAPPLPPNKGKVTQASSANTLWKTNSVSDGGRSQRSSDPPAVHPLPLRVSTN 840  
 Db 781 TTSAPPLPPNKGKVTQASSANTLWKTNSVSDGGRSQRSSDPPAVHPLPLRVSTN 840  
 QY 841 PLTPTPPPPVAKTPSVMEALSQSKPAPGISOIRPPPLPPOPSRLPQKPPAGTDKST 900  
 Db 841 PLTPTPPPPVAKTPSVMEALSQSKPAPGISOIRPPPLPPOPSRLPQKPPAGTDKST 900  
 QY 901 PLTNKGQPRGPDLSATEALGPLSNAMVLQPPAPMPKRSQATKLPKRVKALYNCVADNP 960  
 Db 901 PLTNKGQPRGPDLSATEALGPLSNAMVLQPPAPMPKRSQATKLPKRVKALYNCVADNP 960  
 QY 961 DELTFSEGVDVIIVDGEDQEWIIGHIDGDPGRKGAFFVSVHFIAID 1006  
 Db 961 DELTFSEGVDVIIVDGEDQEWIIGHIDGDPGRKGAFFVSVHFIAID 1006

RESULT 3  
 AAW77288  
 ID AAW77288 standard; protein; 982 AA.  
 XX  
 AC AAW77288;  
 XX  
 AC  
 DT 17-OCT-2003 (revised)  
 DT 20-NOV-1998 (first entry)  
 XX  
 XX Zebrafish differentiation enhancing factor 2 protein.  
 DE  
 DE Zebrafish; differentiation enhancing factor; ankyrin repeat; C2 domain;  
 KW SH3 consensus binding sequence; pleckstrin homology domain; adipogenesis;  
 KW neurogenesis; hyperplastic disease; neoplastic disease; nervous system.  
 XX  
 OS Danio rerio.  
 XX  
 PN W09836065-A1.  
 XX

PD 20-AUG-1998.  
 XX  
 PF 13-FEB-1998; 98MO-US002724.  
 XX  
 PR 14-FEB-1997; 97US-0038191P.  
 XX  
 PA (DAND ) DANA FARBER CANCER INST INC.  
 XX  
 PI Thomas RM, King FJ, Harris DF, Hu E, Spiegelman B, Chan J;  
 XX WPI; 1998-457173/40.  
 DR N-PSDB; AAVS9105.  
 XX  
 PT New nucleic acid encoding differentiation enhancing factor - used  
 PT particularly to regulate adipogenesis and neurogenesis, e.g. for treating  
 PT tumours and neurological disease.  
 XX  
 PS Claim 3; Fig 12; 203pp; English.  
 XX  
 CC The differentiation enhancing factors (DEF), comprise at least one each  
 CC of SH3 consensus binding sequence, ankyrin repeat, pleckstrin homology  
 CC domain and C2 domain. The DEF induce adipogenesis or neurogenesis; they  
 CC are mediators of SH3-domain dependent signalling and may be involved in  
 CC cellular gene expression, cytoskeletal architecture, protein trafficking,  
 CC endocytosis or adhesion, migration, proliferation and differentiation of  
 CC cells. Typical applications of DEF and agents that modulate interaction of  
 CC between the protein and it's ligand, or of nucleic acid expressing them,  
 CC are treatment of hyperplastic and neoplastic disease (a wide range of  
 CC solid tumours and leukaemias), including metastases; for in vitro  
 CC induction of differentiation of neural crest cells to neurons, glial  
 CC cells etc.; for increasing neuron survival, and inducing cell repair, in  
 CC the nervous system (e.g. treatment of traumatic injury, stroke, stroke,  
 CC Alzheimer's, Parkinson's or Huntington's diseases, amyotrophic lateral  
 CC sclerosis, multiple sclerosis etc.). (Updated on 17-OCT-2003 to  
 CC standardise OS field)  
 XX  
 SQ Sequence 982 AA;

Query Match 73.5%; Score 3874; DB 2; Length 982;  
 Best Local Similarity 74.1%; Pred. No. 6.4e-264;  
 Matches 755; Conservative 92; Mismatches 122; Indels 50; Gaps 13;  
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 Db 1 MPDQITVAEFVTETNEDYKSPASFTTRMTCRNTVSALEALDVRMVLKMKSVKA 60  
 QY 61 INSSGLAHVNEBEOYTOALEKFGGNCVCRDDPDLSAFLKFSVFTKELTALFKNLONMN 120  
 Db 61 IYASGLAHVNEBEOYTOALEKFGGNCVCRDDPDLSAFLKFSVFTKELTALFKNLONMN 120  
 QY 121 NIISPLDLSLLKGLDKGVKGLKPPDKAWKDYETKITKEKEKHAHKGHMIRTEISG 180  
 Db 121 NIITPLDLSLLKGLDKGVKGLKPPDKAWKDYETKITKEKEKHAHKGHMIRTEISG 180  
 QY 181 ASIASEMEKERRFPOLQMCCEYLLKVNIEIKKGVLLQNLIKYFHAQCNFFQDGLKAVES 240  
 Db 181 ASIASEMEKERRFPOLQMCCEYLLKVNIEIKKGVLLQNLIKYFHAQCNFFQDGLKAVDN 240  
 QY 241 LKPSIETLSTDLHTI KOAQDEERRQLIQLDRILKSAQVEQKEDSQRSTAYSLSHQPOG 300  
 Db 241 LKPSIETLSTDLHTI KOAQDEERRQLIQLDRILKSAQVEQKEDSQRSTAYSLSHQPOG 300  
 QY 301 NKEHGTNRNGSLYKKSQDGIKRVWOKRCSVKNGLFTTISHGTANRPPAKJNLLTCOVKTNP 360  
 Db 301 NKEHGTNRNGSLYKKSQDGIKRVWOKRCSVKNGLFTTISHGTANRPPAKJNLLTCOVKTNP 360  
 QY 361 EEKCFDLISHDRTHYFQAEDEQECQIWMVSLQNSKEEALNNAFKGDDNTGENNIVQELT 420  
 Db 361 EEKCFDLISHDRTHYFQAEDEQECQIWMVSLQNSKEEALNNAFKGDDNTGENNIVQELT 420  
 QY 421 KEIISEVORMTGNDVCCDCCGAPDPTWLSNLGILTCIECSGIRHRELGVHSPMOSLTLDV 480  
 Db 421 KAILGEVVRMAGNDVCCDCCGAPDPTWLSNLGILTCIECSGIRHRELGVHSPMOSLTLDV 480

GenCore version 5.1.1.6  
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OM protein - protein search, using sw model

Run on: April 18, 2005, 18:42:21 ; Search time 87.3111 Seconds  
(without alignments)  
4456.258 Million cell updates/sec

Title: US-09-914-042-1  
Perfect score: 5273  
Sequence: 1 MPDQISVFSEFAETHDYKA.....DGDPCRGAFFVSVFHFAD 1006

Scoring table: BLOSUM62  
Gapop 10.0 , Gapext 0.5

Searched: 2105692 seqs, 386760381 residues

Total number of hits satisfying chosen parameters: 2105692

Minimum DB seq length: 0  
Maximum DB seq length: 2000000000

Post-processing: Minimum Match 0%  
Maximum Match 100%  
Listing first 45 summaries

Database : A\_Geneseq\_16Dec04:.\*  
1: Geneseq1980s:.\*  
2: Geneseq1990s:.\*  
3: Geneseq2000s:.\*  
4: Geneseq2001s:.\*  
5: Geneseq2002s:.\*  
6: Geneseq2003as:.\*  
7: Geneseq2003bs:.\*  
8: Geneseq2004s:.\*

Pred. No. is the number of results predicted by chance to have a score greater than or equal to the score of the result being printed, and is derived by analysis of the total score distribution.

SUMMARIES

Result No.	Score	Match	Length	DB	ID	Description
1	5253	99.6	1006	2	AAW77290	Aaw77290 Human dif
2	5084	96.4	1006	3	AAB23647	Aab23647 Human Pap
3	3874	73.5	982	2	AAW77288	Aaw77288 Zebrafish
4	3710.5	70.4	783	3	AAB23648	Aab23648 Murine Pa
5	3155	59.8	903	2	AAW77289	Aaw77289 Zebrafish
6	3029	57.4	1072	7	ADD71162	Add71162 Human int
7	3024.5	57.4	1129	7	ADD71155	Add71155 Human int
8	3013.5	57.1	1129	2	AAW77286	Aaw77286 Bovine di
9	3011	57.1	1090	6	AAB38437	Aab38437 Mouse ASA
10	3006	57.0	1132	8	ADJ51009	Adj51009 Human nov
11	3000.5	56.9	1147	6	AAB38436	Aab38436 Mouse ASA
12	2954.5	56.0	1151	2	AAW77287	Aaw77287 Zebrafish
13	2852	54.1	1087	8	ADS34461	Ads34461 POSH prot
14	2465.5	46.8	956	8	ADS34457	Ads34457 POSH prot
15	2410	45.7	949	8	ADS34458	Ads34458 POSH prot
16	2369	44.9	940	8	ADS10772	Ads10772 Human the
17	2363	44.8	940	4	AAW40068	Aaw40068 Human pol
18	2071.5	39.3	903	7	ADB64797	Adb64797 Human pro
19	2071.5	39.3	903	7	ADK81947	Adk81947 Hepatocel
20	1801.5	34.2	350	4	AAU87117	Aau87117 Novel cen
21	1801.5	34.2	350	8	AD154432	Ad154432 Novel hum
22	1759.5	33.4	349	4	AAU87438	Aau87438 Novel cen
23	1759.5	33.4	349	8	AD154753	Ad154753 Novel hum
24	1695.5	32.2	1020	4	ABB58971	Abb58971 Drosophil
25	1075.5	20.4	208	7	ADB64130	Adb64130 Human pro

26	802	15.2	459	4	AAU20370	Aau20370 Human sec
27	611.5	11.6	358	7	ADJ71009	Adj71009 Human hea
28	579	11.0	407	5	ABB97460	Abb97460 Novel hum
29	573.5	10.9	778	7	ADD71161	Add71161 Human int
30	571.5	10.8	778	4	AAW39122	Aaw39122 Human pol
31	569	10.8	407	6	ABU70671	Abu70671 Human adi
32	562	10.7	799	4	ABG17242	Abg17242 Novel hum
33	558	10.6	764	6	ABU52617	Abu52617 Human NOV
34	551	10.4	804	5	ABB97954	Abb97954 Human pro
35	532.5	10.1	805	4	AAW40908	Aaw40908 Human pol
36	530.5	10.1	958	8	ADS10512	Ads10512 Human the
37	529	10.0	834	5	ABG91802	Abg91802 Human int
38	529	10.0	834	5	AAU99904	Aau99904 Human 468
39	509	9.7	740	8	ADS34455	Ads34455 POSH prot
40	480	9.1	156	4	ABB11268	Abb11268 Human dif
41	439	8.3	828	4	ABB62649	Abb62649 Drosophil
42	422.5	8.0	560	4	AAE07122	Aae07122 Human gen
43	419	7.9	605	5	ABG93808	Abg93808 Transcrip
44	419	7.9	605	5	AAU71799	Aau71799 Zinc fing
45	412	7.8	176	4	AAW41854	Aaw41854 Human pol

ALIGNMENTS

RESULT 1  
AAW77290  
ID AAW77290 standard; protein; 1006 AA.  
XX  
AC AAW77290;  
XX  
DT 20-NOV-1998 (first entry)  
XX  
DE Human differentiation enhancing factor 2 gene.  
XX  
KW Human; differentiation enhancing factor; ankyrin repeat; C2 domain;  
KW SH3 consensus binding sequence; pleckstrin homology domain; adipogenesis;  
KW neurogenesis; hyperplastic disease; neoplastic disease; nervous system.  
XX  
OS Homo sapiens.  
XX  
PN WO9836065-A1.  
XX  
PD 20-AUG-1998.  
XX  
PF 13-FEB-1998; 98WO-US002724.  
XX  
PR 14-FEB-1997; 97US-0038191P.  
XX  
PI (DAND ) DANA FARBER CANCER INST INC.  
XX  
PI Thomas RM, King FJ, Harris DF, Hu E, Spiegelman B, Chan J;  
XX  
WPI; 1998-467173/40.

Exhibit A

New nucleic acid encoding differentiation enhancing factor - used particularly to regulate adipogenesis and neurogenesis, e.g. for treating tumours and neurological disease.  
Example 13; Fig 12; 203pp; English.

The differentiation enhancing factors (DEF), comprise at least one each of SH3 consensus binding sequence, ankyrin repeat, pleckstrin homology domain and C2 domain. The DEF induce adipogenesis or neurogenesis; they are mediators of SH3-domain dependent signalling and may be involved in cellular gene expression, cytoskeletal architecture, protein trafficking, endocytosis or adhesion, migration, proliferation and differentiation of cells. Typical applications of DEF and agents that modulate interaction between the protein and it's ligand, or of nucleic acid expressing them, are treatment of hyperplastic and neoplastic disease (a wide range of solid tumours and leukemias), including metastases; for in vitro induction of differentiation of neural crest cells to neurons, glial cells etc.; for increasing neuron survival, and inducing cell repair, in

CC the nervous system (e.g. treatment of traumatic injury, stroke,  
 CC Alzheimer's, Parkinson's or Huntington's diseases, amyotrophic lateral  
 CC sclerosis, multiple sclerosis etc.)  
 XX Sequence 1006 AA;

Query Match  
 Best Local Similarity 99.6%; Score 5253; DB 2; Length 1006;  
 Matches 1003; Conservative 0; Mismatches 3; Indels 0; Gaps 0;

QY 1 MPQISVSFVAETHEDYKAPTASSFTTRTAQCRNTVAALAEALDVRMVLKMKSVKA 60  
 DB 1 MPQISVSFVAETHEDYKAPTASSFTTRTAQCRNTVAALAEALDVRMVLKMKSVKA 60  
 QY 61 INSSGLAHVENEEOYTOALEKFGGNCVCRDDPDLGSAFLKFSVFTKELTALFKNLQNN 120  
 DB 61 INSSGLAHVENEEOYTOALEKFGGNCVCRDDPDLGSAFLKFSVFTKELTALFKNLQNN 120  
 QY 121 NIISFPLDLSLLKGDGKGVKDLKPKFPAKWDYETIKITKEKEKSHAKLHGMIRTEISG 180  
 DB 121 NIISFPLDLSLLKGDGKGVKDLKPKFPAKWDYETIKITKEKEKSHAKLHGMIRTEISG 180  
 QY 181 ASIAEMEKEKRRFFPOLQNCVYLLKNEIKIKGVLDLQNLKIFHAQCNFFODGLKAVES 240  
 DB 181 ASIAEMEKEKRRFFPOLQNCVYLLKNEIKIKGVLDLQNLKIFHAQCNFFODGLKAVES 240  
 QY 241 LKPSIETLSTDLHTTIKQADEERRQIOLRDLKLSALQVEKEDSQIRQSTAYSILHPOG 300  
 DB 241 LKPSIETLSTDLHTTIKQADEERRQIOLRDLKLSALQVEKEDSQIRQSTAYSILHPOG 300  
 QY 301 NKEHGTENGSLYKSDGIRKWKRCVKNGLTISHGTANRPPAKNLILTCQVKNP 360  
 DB 301 NKEHGTENGSLYKSDGIRKWKRCVKNGLTISHGTANRPPAKNLILTCQVKNP 360  
 QY 361 EEKCFDLISHDRTHYFOADEQSCQIWMVLSQNSKEALNNAFKGDDNTGENNIVBELT 420  
 DB 361 EEKCFDLISHDRTHYFOADEQSCQIWMVLSQNSKEALNNAFKGDDNTGENNIVBELT 420  
 QY 421 KEIISVQRTGNDVCCGAPDPTWLSTNLGILTCIECSIHELGVHSPQMSLTLDV 480  
 DB 421 KEIISVQRTGNDVCCGAPDPTWLSTNLGILTCIECSIHELGVHSPQMSLTLDV 480  
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 DB 481 LGTSELLAKNIGNAGFNEIMECCLPAEDSVKPNPGSDMNAKDYITAKVIERYARKKH 540  
 QY 541 ADNAAKLHSLCEAVKTRDIFGLLOAVADGVDTLTKIPLANGHEPDTALHLAVRSVDRTS 600  
 DB 541 ADNAAKLHSLCEAVKTRDIFGLLOAVADGVDTLTKIPLANGHEPDTALHLAVRSVDRTS 600  
 QY 601 LHVDPLVQNSGNDKQTKGKSTALHYCCLTDAECLKLLRGKASIBIANESGETPLDI 660  
 DB 601 LHVDPLVQNSGNDKQTKGKSTALHYCCLTDAECLKLLRGKASIBIANESGETPLDI 660  
 QY 661 AKRLKHECEELLTQALSGRNSHVHVEYWRLLHEDLDESDDMDKLOPSENREDRP 720  
 DB 661 AKRLKHECEELLTQALSGRNSHVHVEYWRLLHEDLDESDDMDKLOPSENREDRP 720  
 QY 721 ISFYOLGNSQIQSNAVSLARDAANLAKKORAFMPSILQNETYGALLSGSPPPAQAAPS 780  
 DB 721 ISFYOLGNSQIQSNAVSLARDAANLAKKORAFMPSILQNETYGALLSGSPPPAQAAPS 780  
 QY 781 TTSAPPLPPRNVGKVQTASSANTLWKTNSVSDGSRQSSDDPPVHPPLPLRLVTSTN 840  
 DB 781 TTSAPPLPPRNVGKVQTASSANTLWKTNSVSDGSRQSSDDPPVHPPLPLRLVTSTN 840  
 QY 841 PLTPTPPPPVAKTPSWNEALSQSKPAPPGISQIRPPPLPPQPSRLPOKKPACDTKST 900  
 DB 841 PLTPTPPPPVAKTPSWNEALSQSKPAPPGISQIRPPPLPPQPSRLPOKKPACDTKST 900  
 QY 901 PLTNKQPPRPVDSLATEALGPLSNAMVLOPPAMPKRSQATKLPKRVKALYNCVADNP 960  
 DB 901 PLTNKQPPRPVDSLATEALGPLSNAMVLOPPAMPKRSQATKLPKRVKALYNCVADNP 960

QY 961 DELTFSEGDVIIVDGEEDQEWNIHIDGIDGPRKGAFFVSVFHTIAD 1006  
 DB 961 DELTFSEGDVIIVDGEEDQEWNIHIDGIDGPRKGAFFVSVFHTIAD 1006

RESULT 2  
 AAB23647  
 ID AAB23647 standard; protein; 1006 AA.  
 XX AAB23647;  
 AC AAB23647;  
 XX  
 DT 05-JAN-2001 (first entry)  
 XX  
 DE Human Pap-DELTA protein sequence SEQ ID NO:1.  
 XX

KW Pap; Pyk2 binding protein; Pyk2 C-terminus associated protein; diagnosis;  
 KW cytosolic; neuroprotective; immunomodulatory; cardioactive; cancer;  
 KW cardiovascular disorder; neurodegenerative disorder; immune disorder.  
 OS Homo sapiens.

XX WO200049144-A2.

XX 24-AUG-2000.

XX 18-FEB-2000; 2000WO-US004647.

XX 22-FEB-1999; 99US-0121125P.

XX (SUGE-) SUGEN INC.

XX Lev S, Schlessinger J, Chen A, Hernandez J, Martinez R;

XX Plowman GD;

XX WPI; 2000-524592/47.

XX Pyk2 binding protein nucleic acids, polypeptides, antibodies and

XX antisense oligonucleotides, the oligonucleotides are useful for treating

XX cancer or a cardiovascular, neurodegenerative or immune disorder.

XX Claim 15; Fig 1; 132pp; English.

XX The present sequence represents the human Pap-DELTA protein. Pap is a

XX Pyk2 C-terminal associated protein (Pyk2 binding protein). Pap proteins

XX have cytostatic, neuroprotective, immunomodulatory and cardioactive

XX activities. Pyk2 binding protein, immunomodulatory and cardioactive

XX diagnostic agents for the detection of diseases. Oligonucleotides from

XX polynucleotide sequences encoding Pap proteins may be useful for the

XX treatment of diseases such as cancer or a cardiovascular,

XX neurodegenerative or immune disorder.

XX Sequence 1006 AA;

QY Query Match

DB Best Local Similarity 96.4%; Score 5084; DB 3; Length 1006;

QY Matches 983; Conservative 0; Mismatches 23; Indels 0; Gaps 0;

DB 1 MPQISVSFVAETHEDYKAPTASSFTTRTAQCRNTVAALAEALDVRMVLKMKSVKA 60

QY 61 INSSGLAHVENEEOYTOALEKFGGNCVCRDDPDLGSAFLKFSVFTKELTALFKNLQNN 120

DB 61 INSSGLAHVENEEOYTOALEKFGGNCVCRDDPDLGSAFLKFSVFTKELTALFKNLQNN 120

QY 121 NIISFPLDLSLLKGDGKGVKDLKPKFPAKWDYETIKITKEKEKSHAKLHGMIRTEISG 180

DB 121 NIISFPLDLSLLKGDGKGVKDLKPKFPAKWDYETIKITKEKEKSHAKLHGMIRTEISG 180

QY 181 ASIAEMEKEKRRFFPOLQNCVYLLKNEIKIKGVLDLQNLKIFHAQCNFFODGLKAVES 240

DB 181 ASIAEMEKEKRRFFPOLQNCVYLLKNEIKIKGVLDLQNLKIFHAQCNFFODGLKAVES 240

QY 241 LKPSIETLSLTLHTIKQAQDEERRQLIQRLDILKSAQVQKEDSQIRQSTAYSLHQPOG 300  
 Db |||||  
 QY 241 LKPSIETLSLTLHTIKQAQDEERRQLIQRLDILKSAQVQKEDSQIRQSTAYSLHQPOG 300  
 Db |||||  
 QY 301 NKEHGTNRSLYKSGDGIKRWKRCVKNGLTTSHTGTANRPPAKNLTLCOVKTNP 360  
 Db |||||  
 QY 301 NKEHGTNRSLYKSGDGIKRWKRCVKNGLTTSHTGTANRPPAKNLTLCOVKTNP 360  
 Db |||||  
 QY 361 EEKCFDLISHDRTHYFQAEDQECQIWMVSLQNSKEEALNNAFKGDDNTGENNIVQELT 420  
 Db |||||  
 QY 361 EEKCFDLISHDRTHYFQAEDQECQIWMVSLQNSKEEALNNAFKGDDNTGENNIVQELT 420  
 Db |||||  
 QY 421 KEIISVQRTMGNDVCCGAPDPTWLSNLGILTCIECSGIRHGLGVHSPQSLTLDV 480  
 Db |||||  
 QY 421 KEIISVQRTMGNDVCCGAPDPTWLSNLGILTCIECSGIRHGLGVHSPQSLTLDV 480  
 Db |||||  
 QY 481 LGTSELLAKNIGNAGNEIWECLPAEDSVKPNFGSDMNAKDYITAKYIERRYARKKH 540  
 Db |||||  
 QY 481 LGTSELLAKNIGNAGNEIWECLPAEDSVKPNFGSDMNAKDYITAKYIERRYARKKH 540  
 Db |||||  
 QY 541 ADNAALHLSICEAVKTRDIFGLQAYADGVDLTEKIPLANGHEPDETALHLAVRSVDRTS 600  
 Db |||||  
 QY 541 ACNAALHLSICEAVKTRDIFGLQAYADGVDLTEKIPLANGHEPDETALHLAVRSVDRTS 600  
 Db |||||  
 QY 601 LHIVDFLVQNSGNDKQTKGKSTALHYCCLTDAECLKLLRGKASIEIANESGETPLDI 660  
 Db |||||  
 QY 601 LHIVDFLVQNSGNDKQTKGKSTALHYCCLTDAECLKLLRGKASIEIANESGETPLDI 660  
 Db |||||  
 QY 661 AKRLKHECHELLTOALSGRPNHSHVYEWRLHEDLDESDDDMDKLOPSENREDRP 720  
 Db |||||  
 QY 661 AKRLKHECHELLTOALSGRPNHSHVYEWRLHEDLDESDDDMDKLOPSENREDRP 720  
 Db |||||  
 QY 721 ISFYQLGSLQNSLQNAVSLAADAANLAKEKORAFMPSILQNETYCALLSGSPPPAQAAPS 780  
 Db |||||  
 QY 721 ISFYQLGSLQNSLQNAVSLAADAANLAKEKORAFMPSILQNETYCALLSGSPPPAQAAPS 780  
 Db |||||  
 QY 781 TTSAPPLPPRNVGKVQTASSANTLWKTNSVSDGGRSQRSSDPPAVHPLPLRVSTN 840  
 Db |||||  
 QY 781 TTSAPPLPPRNVGKVQTASSANTLWKTNSVSDGGRSQRSSDPPAVHPLPLRVSTN 840  
 Db |||||  
 QY 841 PLTPPTPPPVAKTPSVEALSQSKPAPPGISQIRPPPLPQPPSRLPQKKPAPGTDKST 900  
 Db |||||  
 QY 841 PLTPPTPPPVAKTPSVEALSQSKPAPPGISQIRPPPLPQPPSRLPQKKPAPGTDKST 900  
 Db |||||  
 QY 901 PLTNKGOPRGPVDSLATEALGPLSNAMVLOPPAPMPRKSOATKLKPRVKALYNCVADNP 960  
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 QY 901 PLTNKGOPRGPVDSLATEALGPLSNAMVLOPPAPMPRKSOATKLKPRVKALYNCVADNP 960  
 Db |||||  
 QY 961 DELTFSEGDIIVDGEEDQEWIGHIDGDPGRKGAFFVSVFHIAD 1006  
 Db |||||  
 QY 961 DELTFSEGDIIVDGEEDQEWIGHIDGDPGRKGAFFVSVFHIAD 1006  
 Db |||||

RESULT 3  
 AAW77288  
 ID AAW77288 standard; protein; 982 AA.  
 XX  
 AC AAW77288;  
 AC  
 DX  
 DT 17-OCT-2003 (revised)  
 DT 20-NOV-1998 (first entry)  
 XX  
 DE Zebrafish differentiation enhancing factor 2 protein.  
 XX  
 KW Zebrafish; differentiation enhancing factor; ankyrin repeat; C2 domain;  
 KW SH3 consensus binding sequence; pleckstrin homology domain; adipogenesis;  
 KW neurogenesis; hyperplastic disease; neoplastic disease; nervous system.  
 XX  
 OS Danio rerio.  
 XX  
 PN W09836065-A1.  
 XX

PD 20-AUG-1998.  
 XX 13-FEB-1998; 98WO-US002724.  
 PR 14-FEB-1997; 97US-0038191P.  
 XX (DAND ) DANA FARBER CANCER INST INC.  
 PA Thomas RM, King FJ, Harris DF, Hu E, Spiegelman B, Chan J;  
 PI WPI; 1998-467173/40.  
 XX N-PSDB; AAV59105.  
 DR  
 XX  
 PT New nucleic acid encoding differentiation enhancing factor - used  
 PT particularly to regulate adipogenesis and neurogenesis, e.g. for treating  
 PT tumours and neurological disease.  
 XX  
 PS Claim 3; Fig 12; 203pp; English.  
 XX  
 CC The differentiation enhancing factors (DEF), comprise at least one each  
 CC of SH3 consensus binding sequence, ankyrin repeat, pleckstrin homology  
 CC domain and C2 domain. The DEF induce adipogenesis or neurogenesis; they  
 CC are mediators of SH3-domain dependent signalling and may be involved in  
 CC cellular gene expression, cytoskeletal architecture, protein trafficking,  
 CC endocytosis or adhesion, migration, proliferation and differentiation of  
 CC cells. Typical applications of DEF and agents that modulate interaction of  
 CC between the protein and it's ligand, or of nucleic acid expressing them,  
 CC are treatment of hyperplastic and neoplastic disease (a wide range of  
 CC solid tumours and leukaemias), including metastases; for in vitro  
 CC induction of differentiation of neural crest cells to neurons, glial  
 CC cells etc.; for increasing neuron survival, and inducing cell repair, in  
 CC the nervous system (e.g. treatment of traumatic injury, stroke,  
 CC Alzheimer's, Parkinson's or Huntington's diseases, amyotrophic lateral  
 CC sclerosis, multiple sclerosis etc.). (Updated on 17-OCT-2003 to  
 CC standardise OS field)  
 XX  
 SQ Sequence 982 AA;  
 Query Match 73.5%; Score 3874; DB 2; Length 982;  
 Best Local Similarity 74.1%; Pred. No. 6.4e-264;  
 Matches 755; Conservative 92; Mismatches 122; Indels 50; Gaps 13;  
 QY 1 MPDQISVSFFVAETHEDYKAPTASSFTTTRACRNTVAAIEEALDVRMVLKMKKSVKA 60  
 Db |||||  
 QY 1 MPDQITVAEFVTETNEDYKSPASFTTTRMTHCRNTVSALEBALDVRSLVKMKKSVKA 60  
 Db |||||  
 QY 61 INSSGLAHVENEEOYTOALEKFGNCVCRRDDPDLGSAFLKFSVFTKELTALFKNLQNN 120  
 Db |||||  
 QY 61 IVASGLAHVENEEOYTOALEKFGNCVCRRDDPDLGSAFLKFSVFTKELTALFKNLQNN 120  
 Db |||||  
 QY 121 NIISFPLDLSLLKGLDKGVKDLKPKPDKAWKDYETKITKEKEKHAHLGHMIRTEISG 180  
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 QY 121 NIITPFLDLSLLKGLDKGVKDLKPKPDKAWKDYETKITKEKEKHAHLGHMIRTEISG 180  
 Db |||||  
 QY 181 ABIAEMEKEKRRFFOLQMCCEYLLKVNIEIKIKGVLDLQNLIKYFHAQCNFFQDGLKAVES 240  
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 QY 181 ABIAEMEKEKRRFFOLQMCCEYLLKVNIEIKIKGVLDLQNLIKYFHAQCNFFQDGLKAVDN 240  
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 QY 241 LKPSIETLSLTLHTIKQAQDEERRQLIQRLDILKSAQVQKEDSQIRQSTAYSLHQPOG 300  
 Db |||||  
 QY 241 LKPSIEKLTADLHISIKQVQDEERRQLIQRLDILKSAQVQKEDSQIRQSTAYSLHQPOG 300  
 Db |||||  
 QY 301 NKEHGTNRSLYKSGDGIKRWKRCVKNGLTTSHTGTANRPPAKNLTLCOVKTNP 360  
 Db |||||  
 QY 301 NKEHGTNRSLYKSGDGIKRWKRCVKNGLTTSHTGTANRPPAKNLTLCOVKTNP 360  
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 QY 361 EEKCFDLISHDRTHYFQAEDQECQIWMVSLQNSKEEALNNAFKGDDNTGENNIVQELT 420  
 Db |||||  
 QY 361 EEKCFDLISHDRTHYFQAEDQECQIWMVSLQNSKEEALNNAFKGDDNTGENNIVQELT 420  
 Db |||||  
 QY 421 KEIISVQRTMGNDVCCGAPDPTWLSNLGILTCIECSGIRHGLGVHSPQSLTLDV 480  
 Db |||||  
 QY 421 KAILGEVCRMAGNDVCCGAPDPTWLSNLGILTCIECSGIRHGLGVHSPQSLTLDV 480  
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